FEATURES OF THE EARLY PULMONARY INFILTRATION *

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THE greatest obstacle to understanding the behavior of the earliest lesions of pulmonary tuberculosis is their failure to sicken the host. Since, next to absolute prevention of infection, identification and proper management of the early lesion is the most effective means of attack on tuberculosis, the importance of a systematic study of groups of healthy people, among whom the disease may be expected at some future time, can easily be seen. Most published reports include observations of lesions by the x-ray while they are still undetectable by other methods. At Bellevue Hospital a study has been under way for more than thirteen years; the views which I am expressing here are based largely on this experience.

It has been variously stated that a person is unlikely to become a phthisic if he has passed the age of thirty or thirty-five without a demonstrable pulmonary lesion. If we except older people whose resistance has been depleted by uncontrolled diabetes, dietary deficiencies, alcoholism, and the like, the statement holds. Furthermore, it is observed that the lesions of progressive pulmonary tuberculosis usually do not appear until after the start of adolescence. In other words, it is the span of life between adolescence and the early thirties which may be watched with the best prospect of detecting the first appearance of these lesions.

How quickly a lesion may appear in a lung which previously was healthy on x-ray examination is still not very clear. To answer this nearly accurately would require an x-ray examination of a group of healthy young people every week for a number of years; obviously, an objectionable undertaking. However, certain implications are observed. Also, we are not prepared to say much about the relation of the early lesion to recent primary infection. In contrast, with young children, a peculiarity in young white adults, who were tuberculin negative, then became tuberculin positive, and still later developed pulmonary lesions, is the failure to demonstrate by x-ray a typical primary complex; visible enlargement of the regional lymph nodes usually is lacking. Consequently, because the frequency of tuberculin testing must be limited, it is seldom possible to judge clearly whether the lesion discovered is primary, or whether it represents an extension from the primary or an exogenous reinfection.

As to the pathological nature of the early lesion one must depend chiefly upon the interpretation of roentgenographic densities; this must be done with considerable reservation. In a relative minority of instances the pulmonary field, which on previous examination was clear, contains a new, round, discrete, nodular shadow, usually less than a centimeter in diameter, which conforms with that of a productive tubercle. This appearance may be deceptive because the roentgenographic density of small exudative lesions at their start may have little of the collateral haze which is one of the signs of this type of reaction; i.e., there may be a well defined border indicating the limitation of the inflammatory exudate within broncholobular walls rather than the periphery of a productive tubercle. The confusion is not so great in lesions more than a centimeter or so in diameter; first, because the larger the size, the more likely is the process to be wholly or partly of an exudative lobular pneumonic nature; second, because larger lesions usually cast shadows with soft hazy borders. Autopsy of many chronic tuberculous subjects verified the reliability of these criteria, by studying recent lesions of bronchogenic origin, the duration of which is fairly well known from antemortem observation. Thus, the conclusion: most early lesions are predominantly exudative.

Age and race have an important influence. The younger the subject, the more likely is a newly developed lesion to be exudative; this is somewhat more striking in adolescent girls than in boys, and in Negroes than whites. So many observations point this way that one is prompted to utter dictum: until careful observation proves otherwise, assume that a tuberculous lesion, newly developed in the lung of a previously healthy person, is an exudative infiltration and, therefore, potentially very unstable.

The term, infiltration,[1] is aptly applied to the exudative lobular pneumonic or bronchopneumonic lesion. Morphologically, it has the same connotation now as it had when first used by Laennec to distinguish it from the tubercle. The distinction is fundamentally important because of the different potentialities. Whatever the underlying cause may be, the productive (miliary or conglomerate) tubercle tends to follow a mild and indolent course, enlarging and undergoing caseation and excavation slowly; whereas the infiltration (gelatinous or gray) is much more labile, frequently spreading and breaking down rapidly. Similarly the infiltrate may become absorbed much more rapidly than the productive tubercle; or the serous and cellular elements at the periphery of the infiltrate may be absorbed while the liquefied caseous center is excavated.

In retrospect, one may find in a previous roentgenogram a tiny focus which presumably may have been the precursor of the early infiltration, but, without a knowledge of subsequent events, the diagnosis of tubercle, rather than blood vessel, would have been highly imaginative. Nevertheless, there is much to suggest that many recognizable early lesions are in reality extensions from preëxisting occult foci. What we call "early" applies only to that which is demon-

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strable. It is a relative term which once referred to the lesion initiating symptoms, but now, to that casting an identifiable roentgenographic shadow.

Knowing that exudative infiltrations inevitably change progressively or retrogressively, we have paid particular attention to the later evolution of those discovered early. The dominant trend of extensive pneumonic infiltrations to caseation and excavation has been noted by clinicians generally. Small early infiltrations behave in a similar way, the one apparent difference being quantitative; central necrosis is the striking tendency. This is so common as to suggest that almost all early lesions are caseous at the center by the time they can be diagnosed by x-ray. The cavity, when present, is often so minute that it can scarcely be recognized in the roentgenogram; special techniques may be required. That the pinhead or pea-sized rarefactions usually denote excavation is verified by their later enlargement and, as a rule, by the demonstration of tubercle bacilli in the scanty sputum or in the gastric washings upon meticulous examination.

The behavior of the periphery of the early infiltration is conditioned largely upon the rate and extent of the central caseation, the apparent reason being that the former depends upon the rate of manufacture in and local diffusion of toxic substances from the latter. If caseation is minimal and sloughs out early, the peripheral exudate is likely to be absorbed rapidly, and the minute cavity may close promptly; secondary bronchogenic lesions are slight or absent. If caseation is rapid and extensive, peripheral extension is greater; when the liquefied matter is discharged into the bronchial tubes extensive, even lobar pneumonic, secondary lesions may result. If caseation is small or moderate in extent (usually not more than 1 or 2 cm. in cross-section) and becomes arrested with little or no ulceration into the bronchus, the peripheral exudate may be gradually absorbed and organized, encapsulating the cheesy residues; roentgenographically, these often have the appearance of so-called "round infiltrates."

The rate and succession of these changes varies greatly. At the start of our study the usual routine of making roentgenographic observations once a month or so was followed. Soon it was found that some lesions changed markedly in this interval. Now it is routine, upon discovering a newly developed lesion in a previously healthy person, to make the examination every week during the first one or two months. Occasionally an interval of several days is the limit. It has been discovered, especially in adolescent and young adult patients, that a cavity, 2 or 3 cm. in diameter, may appear within a week; and infiltration 1 cm. in diameter may double or triple its size in one to four weeks; an infiltration 1 to 2 cm. in diameter may abruptly discharge its liquefied caseous contents into the bronchi, thus inciting an acute tuberculous lobar pneumonia within two or four weeks. Some early infiltrations remain stationary for weeks or months, then rapidly change with excavation and numerous and extensive secondary lesions. The transition from the early lesion to advanced bilateral disease, in exceptional cases, is a matter of only a few weeks. Resolution, when it occurs, is slow. At first the peripheral exudate, perhaps quite serous, may absorb rapidly but as a rule the process slows as the core of the lesion is approached. In several months minute residues remain, almost naked caseous remnants which may be visualized as collections of myriad organisms, delicately imprisoned, waiting for some passing disturbance to spread them far and wide. The warm, fertile lung is ever receptive for the threatened dissemination. During the subsequent two years, approximately, circumstances decide whether wide destruction is initiated, whether the slow process of fibrous encapsulation may become competent and permanent, or whether an indecisive balance between the forces of destruction and repair leaves the lesions in that uncertain and sad state, known as chronicity.

A most interesting observation is the lag between pathological morphological change and systemic effects. For example, upon first discovering an early infiltration the erythrocyte sedimentation rate usually is reported normal. During the subsequent few weeks a steady or intermittent extension of the lesion, perhaps the excavation, may occur without any coincidental change in this test. Then as the pulmonary involvement continues the sedimentation rate for the first time is accelerated; a few days or weeks later the initial fever may be detected. One may interpret this to mean that the diffusion of toxins must persist and reach a considerable level before the systemic effects are measurable by the ordinary clinical and laboratory tests. In some cases tubercle bacilli are discovered in the sputum before these effects are detected.

Certain implications are suggested. In all probability a tuberculous infiltration may develop in the lung within a few days to several weeks. That this may be the first demonstrable extension from a preëxisting occult focus cannot be denied.

When an infiltration is fresh, with only minimal central caseation, the possibility of resolution and complete healing is greater than it is at any subsequent phase of the disease. Conceivably, conditions would be more favorable if the small caseous core had been extruded, but this seldom occurs without some infection of the surrounding parenchyma.

The opportune time for securing maximal effects of treatment is in this early phase, preferably before there are any severe systemic symptoms and before secondary bronchogenic lesions have had time to develop. To wait for the lesion to give indubitable evidence of its "activity" usually means that the best opportunity for cure

has been lost. Fortunately, this does not imply that an "arrestment" may not occur later. But, to accomplish the most for the patient, the fact must frequently be emphasized and well remembered that a small lesion, demonstrable only by x-ray and wholly symptomless, may be an early infiltration with serious and closely impending potentialities. Unless it is unmistakably fibroid, such a small lesion at the start should be observed roentgenographically at weekly to biweekly intervals. Preferably, the patient should be on rest treatment while this is done. These conceptions have proved, in our experience, to be a sound basis of treatment with results surpassing any other scheme which we have tried. The experience seems to indicate that, if the conceptions could be applied generally, tuberculosis would seldom become the advanced and fatal disease with which, regrettably, we are so familiar.

SUMMARY

The behavior of the earliest lesions of pulmonary tuberculosis can be understood only by a systematic study of apparently healthy people among whom the disease may be expected to appear. The period of life between the start of adolescence and the age of thirty or thirty-five is the time during which most of these lesions first develop.

Most lesions of the early infiltration are a predominantly exudative, lobular pneumonic character; this type of tissue reaction is most conspicuous in adolescents, especially in young girls and in Negroes. The assumption should be made, until well proved otherwise, that this type of reaction prevails, remembering that the roentgenographic appearance may be misleading.

The striking tendency of the early infiltration is to progress to the point of caseation and excavation. Close study demonstrates that such changes may be rapid; e.g., a small lesion may enlarge, caseate, and slough out within a week or two, and give rise to extensive secondary bronchogenic lesions.

Usually, systemic effects such as fever and an accelerated erythrocyte sedimentation rate, are not apparent at the time of the early infiltration and there is often a considerable lag in these effects while the lesion is advancing.

It may be inferred that the early infiltration may develop within a few days or weeks in the lung of a previously healthy person. There is reason to believe that in many or most instances there have been preëxisting occult foci which served as points of origin.

Treatment is most successful if it is based on these conceptions; usually, advanced tuberculosis can be avoided.

1. The term *"infiltration"* refers to the *process* by which the tissue is invaded by tuberculous inflammation, while the term *"infiltrate"* is used to indicate the lesion produced by the process.

HAEMOTOGENOUS PULMONARY MANIFESTATIONS IN EXTRAPULMONARY TUBERCULOSIS*

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TO determine the form of pulmonary pathology existing in association with extrapulmonary tuberculosis, the chest films of 100 unselected patients with extrapulmonary tuberculosis were analyzed.

For comparison and in order to weigh the practical import of results, another 100 cases of routine adult pulmonary tuberculosis, with no evidence of extrapulmonary foci, were reviewed.

In the group of 100 patients with extrapulmonary tuberculosis, 79 showed x-ray evidence of post-primary pulmonary involvement. In 21 of the cases there was no x-ray evidence of a post-primary lesion and in only eight of these there was evidence of primary involvement. Although a certain percentage of primary lesions are hidden behind the mediastinal structures and the domes of the diaphragm, and some of them may have resorbed completely, there is also the possibility of some portal of entry other than the lungs. At any rate the absence of a pulmonary post-primary or primary tuberculous lesion does not necessarily exclude an extrapulmonary focus.

The majority of the pulmonary lesions in the 79 cases were fibrotic and calcific, apparently inactive; proliferative, nodular, and exudative manifestations were decreasingly common in that order. A miliary distribution of lesions was seen in 12 instances, seven of these being acute miliary generalizations and five of chronic nature. Lesions interpreted as of fibrotic character were seen in 37 patients and in 24 of these fibrosis was the predominant feature. Calcification was observed in 35 instances and in 12 of these it was the predominant lesion. The character of these lesions and the tendency toward bilateral, symmetrical, apical and subapical distribution, seen in 44 of the 79 cases indicates a haematogenous origin and emphasizes the systemic nature of the disease.

There was roentgenographic evidence of cavitation in 15 patients. These cavities were mostly thin walled with bilateral symmetrical distribution. In spite of the fact that in 12 cases the sputum was positive for tubercle bacilli and that these patients had pulmonary symptoms, only one had evidence of bronchogenic spread.

In cases in which multiple films were available, stability or regression of the pulmonary lesion and absence of bronchogenic spread were the outstanding features. This was true even of those cases where cavities were present. Though progressive pulmonary lesions did occur, for the

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